

# **EXHIBIT 18**

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(71) Applicant (for all designated States except US):  
**BIOPOLYMER ENGINEERING, INC.** [US/US];  
3388 Mike Collins Drive, Eagan, Minnesota 55121 (US).

(72) Inventor; and

(75) Inventor/Applicant (for US only): **KAREL, Steven, J.** [US/US]; 1562 Park Circle, Mendota, Minnesota 55118 (US).

(74) Agent: **ELRIFI, Ivor, R.**; Mintz, Levin, Cohn, Ferris, Glovsky and Popeo PC, One Financial Center, Boston, Massachusetts 02111 (US).

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(54) Title: COMBINATION OF A BETA-GLUCAN AND AN EGF RECEPTOR ANTAGONIST FOR THE TREATMENT OF CANCER AND INFECTION

(57) Abstract: The present invention encompasses a therapeutic combination composition of a  $\beta$ -glucan EGF receptor antagonist. This therapeutic combination composition is useful for the treatment of diseases including proliferative disorders and immune dysfunction.

## INTERNATIONAL SEARCH REPORT

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INV. A61K36/02 A61K39/395 A61P31/00 A61P35/00

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## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, WPI Data, EMBASE

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2004/030613 A2 (UNIV LOUISVILLE RES FOUNDATION [US]; ROSS GORDON D [US]) 15 April 2004 (2004-04-15) claims page 5, line 17 - page 8, line 2	1-6, 8, 11-19
X	DATABASE WPI Week 200426 Derwent Publications Ltd., London, GB; AN 2004-283158 XP002416577 & WO 2004/026341 A1 (ORIENT CANCER THERAPY CO LTD) 1 April 2004 (2004-04-01) abstract	1, 5, 6, 9, 11-13, 16, 18

 Further documents are listed in the continuation of Box C. See patent family annex.

## \* Special categories of cited documents :

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Date of the actual completion of the international search  25 January 2007	Date of mailing of the international search report  22/02/2007
Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer  Böhmerova, Eva

## INTERNATIONAL SEARCH REPORT

International application No  
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## C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	CHEUNG N-K V ET AL: "Orally administered beta-glucans enhance anti-tumor effects of monoclonal antibodies" CANCER IMMUNOLOGY AND IMMUNOTHERAPY, BERLIN, DE, vol. 51, no. 10, November 2002 (2002-11), pages 557-564, XP002297978 ISSN: 0340-7004 abstract page 559, right-hand column, line 2 - page 560, right-hand column, line 2; figure 1 -----	1,5,6, 11-13, 16,18
X	GELDERMAN KYRA A ET AL: "Complement function in mAb-mediated cancer immunotherapy." TRENDS IN IMMUNOLOGY, vol. 25, no. 3, March 2004 (2004-03), pages 158-164, XP002416499 ISSN: 1471-4906 abstract page 162, right-hand column, last paragraph -----	1,5,6, 13,16
Y	HONG FENG ET AL: "beta-glucan functions as an adjuvant for monoclonal antibody immunotherapy by recruiting tumoricidal granulocytes as killer cells." CANCER RESEARCH, vol. 63, no. 24, 15 December 2003 (2003-12-15), pages 9023-9031, XP002416500 ISSN: 0008-5472 abstract page 9023, right-hand column, last paragraph - page 9024, left-hand column, paragraph 4 page 9030, right-hand column, paragraph 4 -----	1,5-8, 11-13, 16-18
Y	WO 94/04163 A (ALPHA BETA TECHNOLOGY [US]; JAMAS SPIROS [US]; EASSON D DAVIDSON JR [U] 3 March 1994 (1994-03-03) page 1, line 3 - line 23 page 17, line 9 - page 18, line 17 page 20, line 12 - page 21, line 17 examples 1,7,9 claims -----	1-20
Y	US 5 488 040 A (JAMAS SPIROS [US] ET AL) 30 January 1996 (1996-01-30) column 3, line 26 - column 4, line 16; examples 1,6,7 column 10, line 45 - line 60 claims -----	1-20
		-/-

## INTERNATIONAL SEARCH REPORT

International application No  
PCT/US2006/017065

## C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	BROWN G D ET AL: "FUNGAL BETA-GLUCANS AND MAMMALIAN IMMUNITY" IMMUNITY, CELL PRESS, US, vol. 19, no. 3, September 2003 (2003-09), pages 311-315, XP001174145 ISSN: 1074-7613 abstract page 311, right-hand column, last paragraph - page 312, left-hand column, paragraph 3 -----	1-20
Y	BOHN J A ET AL: "(1@rarr 3)-beta-d-Glucans as biological response modifiers: a review of structure-functional activity relationships" CARBOHYDRATE POLYMERS, APPLIED SCIENCE PUBLISHERS, LTD. BARKING, GB, vol. 28, no. 1, 1995, pages 3-14, XP004034425 ISSN: 0144-8617 abstract page 3, right-hand column, line 9 - line 14 page 5, right-hand column, last paragraph -----	1-20
Y	US 6 217 866 B1 (SCHLESSINGER JOSEPH [US] ET AL) 17 April 2001 (2001-04-17) claims column 8, line 2 - column 9, line 19; example IX -----	1-20
Y	"Cetuximab (C225, Erbitux) in combination with irinotecan, infusional 5-fluorouracil (5-FU) and folinic acid (FA) is safe and active in patients (pts) with metastatic colorectal cancer (CRC) expressing epidermal growth factor-receptor (EGFR). Results of a phase I study" EUROPEAN JOURNAL OF CANCER, PERGAMON PRESS, OXFORD, GB, vol. 38, November 2002 (2002-11), pages S148-S149, XP004403940 ISSN: 0959-8049 abstract ----- -/-	1-20

## INTERNATIONAL SEARCH REPORT

International application No  
PCT/US2006/017065

## C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	KIM E S: "CETUXIMAB AS A SINGLE AGENT OR IN COMBINATION WITH CHEMOTHERAPY IN LUNG CANCER" CLINICAL LUNG CANCER, CANCER INFORMATION GROUP, DALLAS, TX, US, vol. 6, no. SUPPL 2, December 2004 (2004-12), pages S80-S84, XP009069948 ISSN: 1525-7304 page S82, right-hand column, paragraph 3 - page S83, left-hand column, paragraph 2 -----	1-20
A	GAWRONSKI MICHAEL ET AL: "Microfibrillar structure of PGG-Glucan in aqueous solution as triple-helix aggregates by small angle x-ray scattering" BIOPOLYMERS, vol. 50, no. 6, November 1999 (1999-11), pages 569-578, XP002416555 ISSN: 0006-3525 abstract page 570, left-hand column page 577, right-hand column, paragraph 1 -----	1-20
P,X	US 2006/009419 A1 (ROSS GORDON D [US] ET AL) 12 January 2006 (2006-01-12) claims paragraphs [0010] - [0020] -----	1-20
E	WO 2006/083458 A (BIORESPONSE LLC [US]; ZELIGS MICHAEL A [US]) 10 August 2006 (2006-08-10) paragraphs [0019], [0021], [0067], [0068]; claims 1,2,24 -----	1,5-8, 11-13, 16-18
E	US 2006/165700 A1 (OSTROFF GARY R [US] ET AL) 27 July 2006 (2006-07-27) claims paragraphs [0010] - [0019] -----	1-20

**INTERNATIONAL SEARCH REPORT**

Information on patent family members

 International application No  
**PCT/US2006/017065**

Patent document cited in search report		Publication date		Patent family member(s)		Publication date
WO 2004030613	A2	15-04-2004		AU 2003268486 A1 AU 2003295326 A1 CA 2496508 A1 CA 2496596 A1 CN 1694715 A CN 1697659 A EP 1536820 A2 EP 1539194 A2 JP 2006502167 T WO 2004021994 A2		29-03-2004 23-04-2004 15-04-2004 18-03-2004 09-11-2005 16-11-2005 08-06-2005 15-06-2005 19-01-2006 18-03-2004
WO 2004026341	A1	01-04-2004		AU 2003264488 A1 EP 1552849 A1 US 2006067947 A1		08-04-2004 13-07-2005 30-03-2006
WO 9404163	A	03-03-1994		AT 210450 T AU 4095397 A AU 679690 B2 AU 5086893 A BR 9307104 A DE 69331324 D1 DE 69331324 T2 EP 0655921 A1 FI 950770 A HU 72418 A2 JP 6107702 A JP 8500623 T JP 2005264167 A NZ 255857 A PL 307567 A1 US 5783569 A US 5622939 A		15-12-2001 18-12-1997 10-07-1997 15-03-1994 30-03-1999 24-01-2002 22-08-2002 07-06-1995 20-02-1995 29-04-1996 19-04-1994 23-01-1996 29-09-2005 28-10-1996 29-05-1995 21-07-1998 22-04-1997
US 5488040	A	30-01-1996		NONE		
US 6217866	B1	17-04-2001		NONE		
US 2006009419	A1	12-01-2006		NONE		
WO 2006083458	A	10-08-2006		NONE		
US 2006165700	A1	27-07-2006		NONE		